Varieties of Forgetfulness

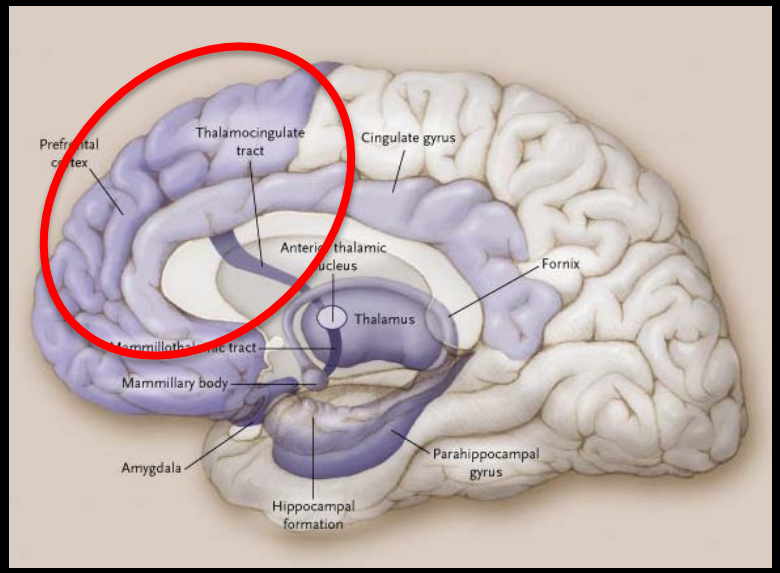
November 12, 2022
Verdugo Hills Hospital
Brain Health Forum

Helena Chui, MD
Alzheimer Disease Research Center
University of Southern California

Varieties of Forgetfulness

- The Memory System
- The Spectrum of Forgetfulness
  - Severity and Causes
  - Prevention and Treatment

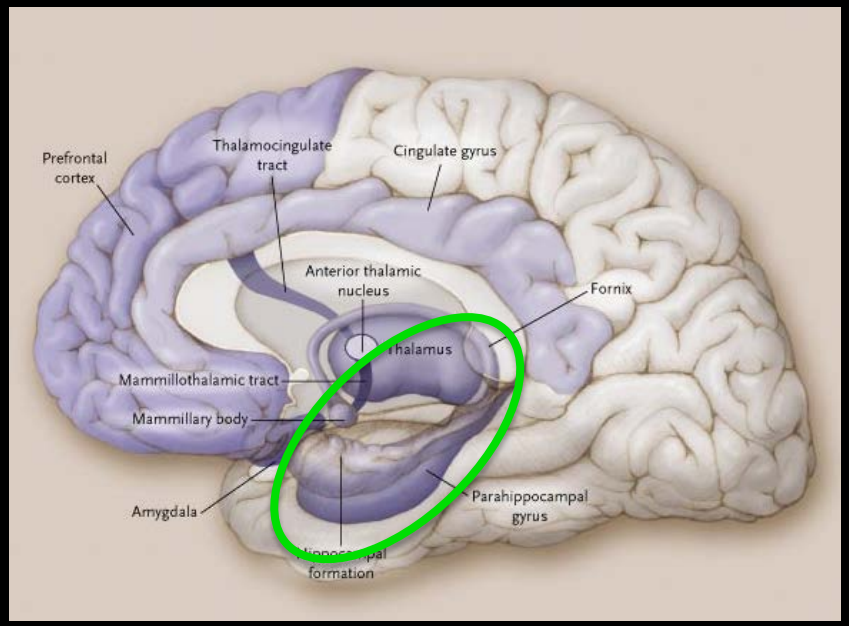
Working Memory – Prefrontal Cortex
Holding small amounts of information in the span of conscious awareness



ATTENTION	Read list of digits (1 digit/ sec.).	Subject has to repeat them in the forward order [ ] 2 1 8 5 4
		Subject has to repeat them in the backward order [ ] 7 4 2
Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors		[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B
Serial 7 subtraction starting at 100	[ ] 93	[ ] 86 [ ] 79 [ ] 72 [ ] 65
		4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

Budson A and Price B. N Engl J Med 2005;352:692-699
Luo L, Craik FI. La Revue Canadienne de psychiatrie 2008: 53: 346

Episodic Memory – Hippocampus
Remembering events and experience that have happened to us personally



Remembering a short story, what you had for dinner last night, and what you did on your last birthday

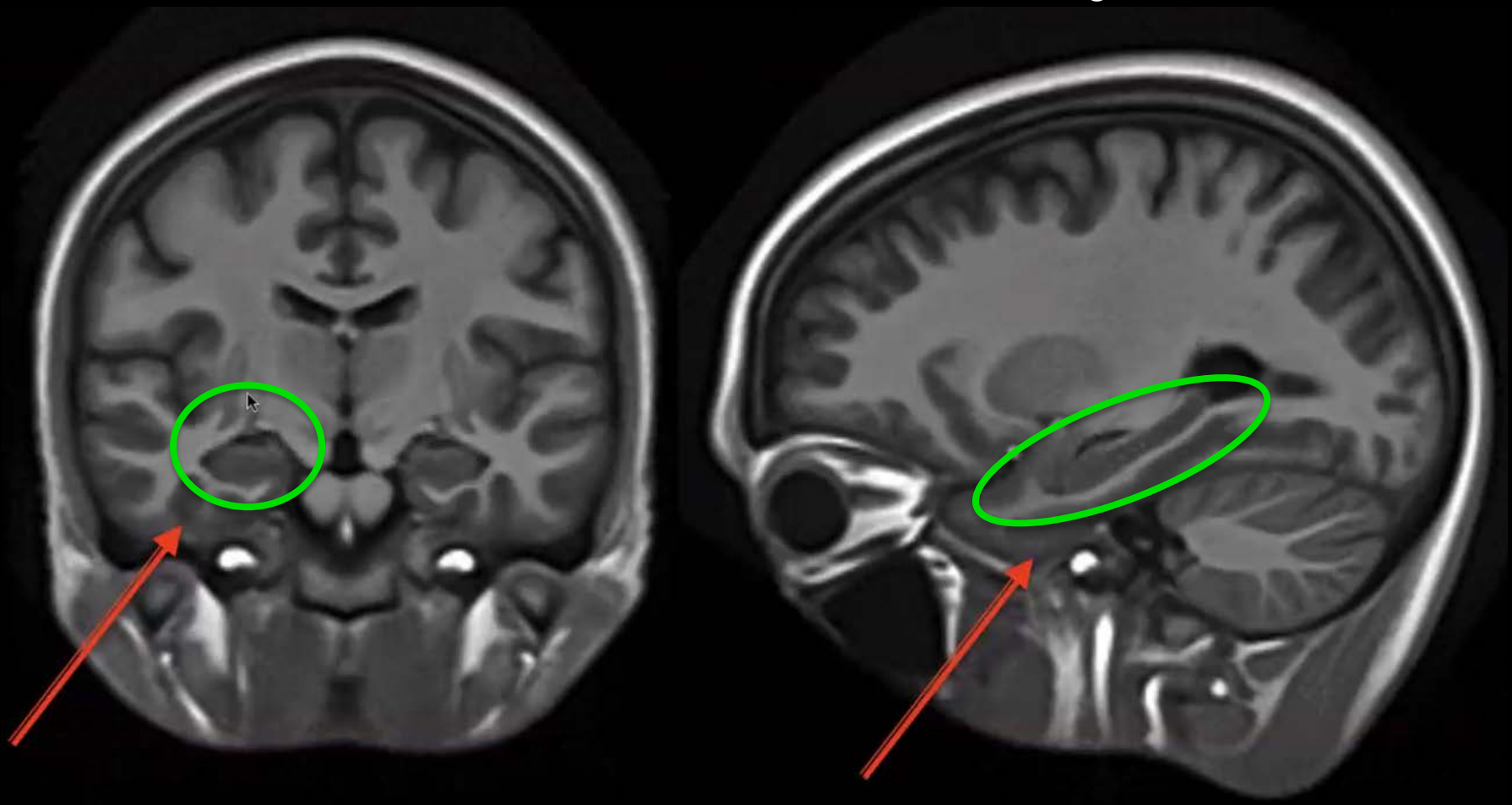
DELAYED RECALL	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only	__/5
Optional	Category cue							
	Multiple choice cue							

Budson A and Price B. N Engl J Med 2005;352:692-699
Luo L, Craik FI. La Revue Canadienne de psychiatrie 2008: 53: 346

Hippocampus

Coronal View

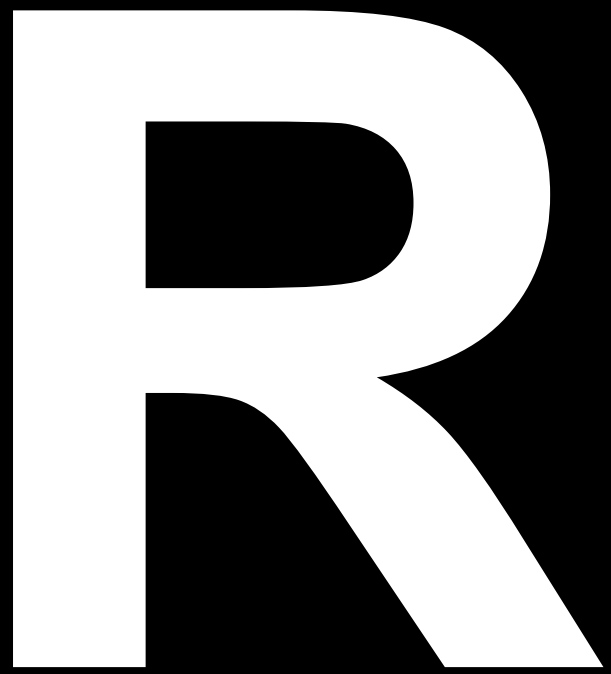
Sagittal View



7T MRI Mark and Betty Stevens Neuroimaging and Informatics Institute

3 R's to Remember

2. Record



1. Register **3. Retrieve**

Varieties of Forgetfulness

- The Memory System
- The Spectrum of Forgetfulness
  - Severity and Causes
  - Prevention and Treatment

Causes of Forgetfulness

Impair Registration/Retrieval

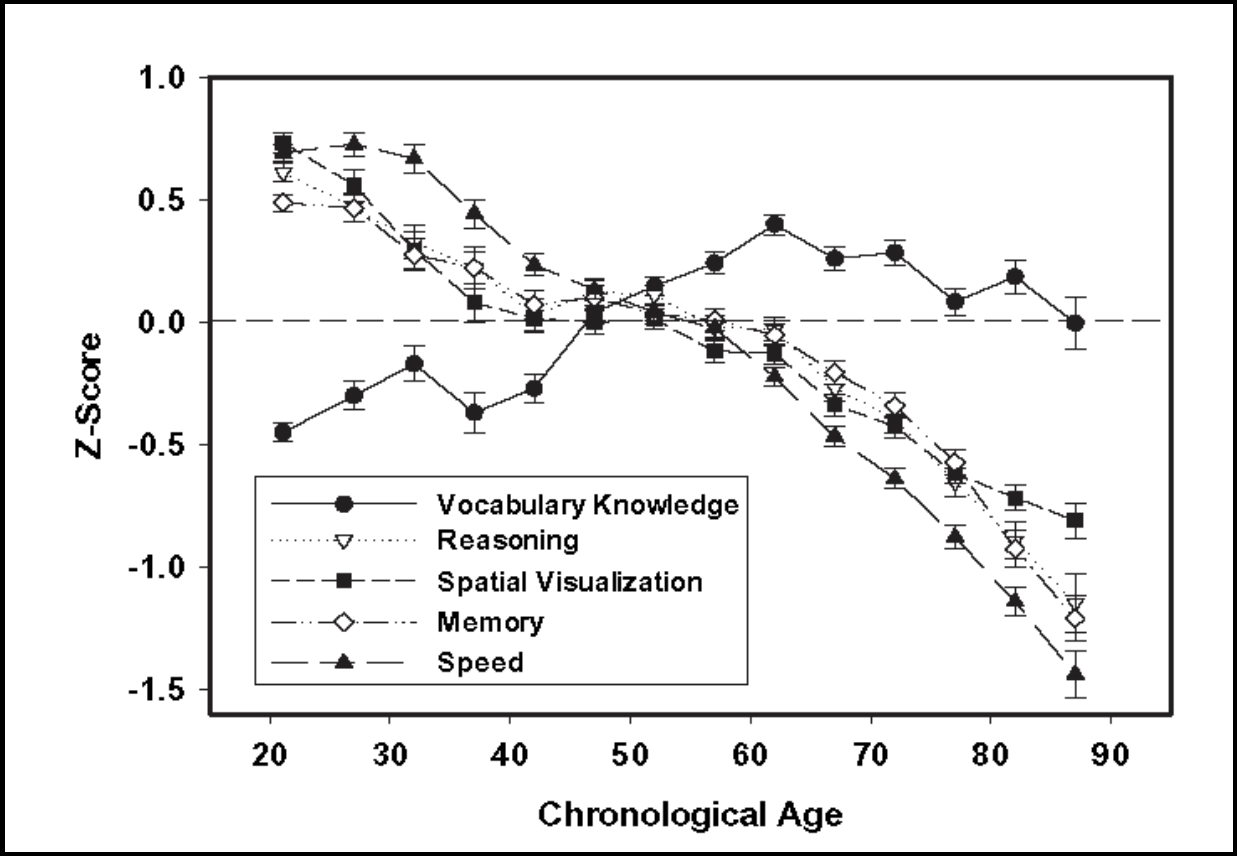
- Normal aging
- Side effects of medication
- Attention deficit disorder
- Obsessive compulsive disorder
- Depression
- Sleep deprivation
- Sleep apnea

Impair Record Button

- Alzheimer disease
- LATE (hippocampal sclerosis)
- Anoxic encephalopathy
- Herpes simplex encephalitis
- Wernicke Korsakoff syndrome (Thiamine deficiency)

LATE = limbic predominant, age-related, TDP-43, encephalopathy

Changes in Cognitive Abilities in Normal Aging

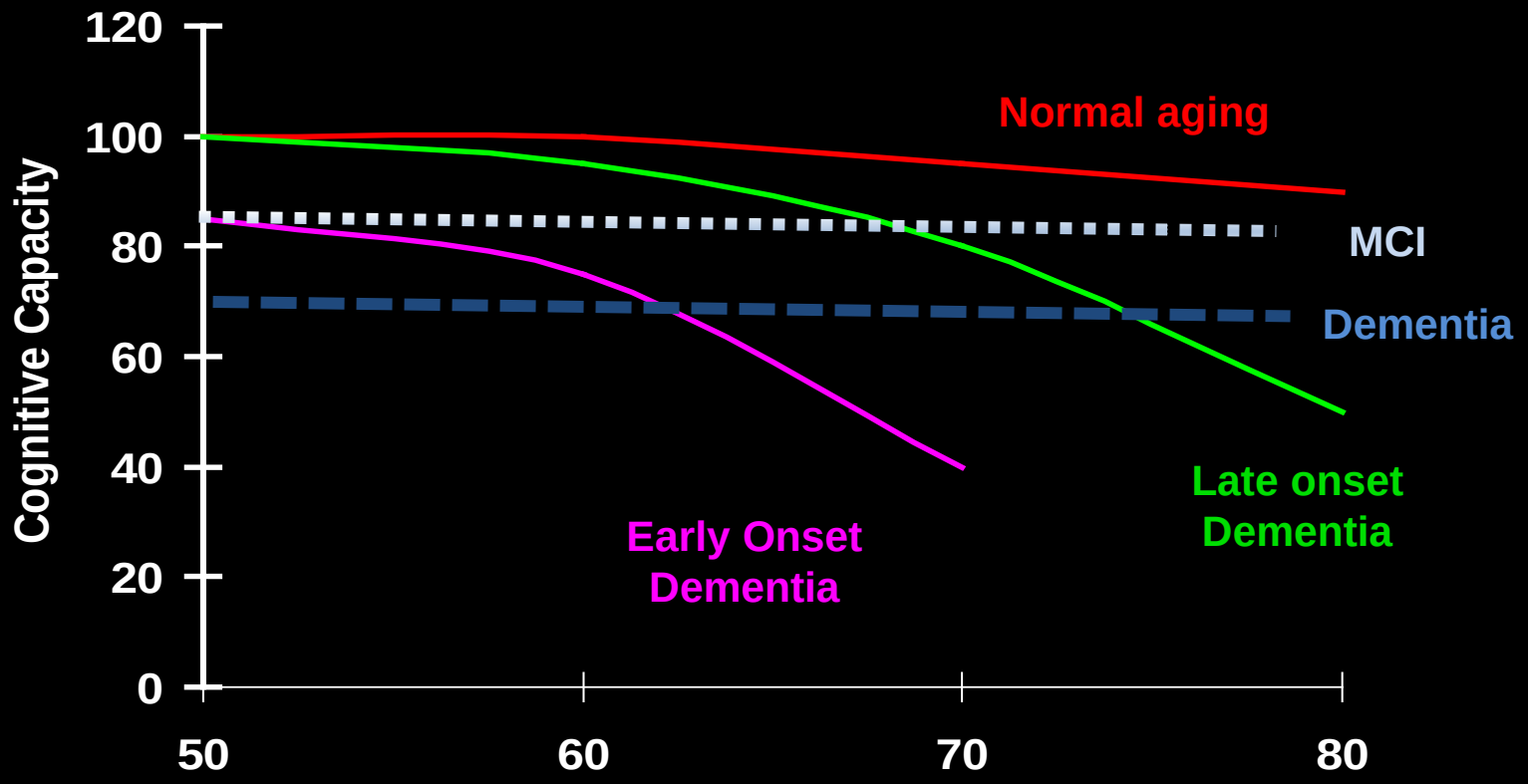


Salthouse, T.A. Nuerobiology of Aging 2009; 30: 507-514

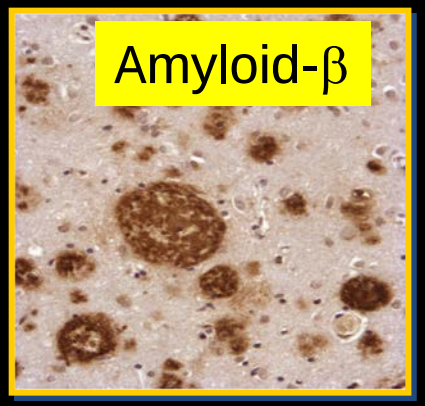
Changes in Cognitive Abilities in Normal Aging

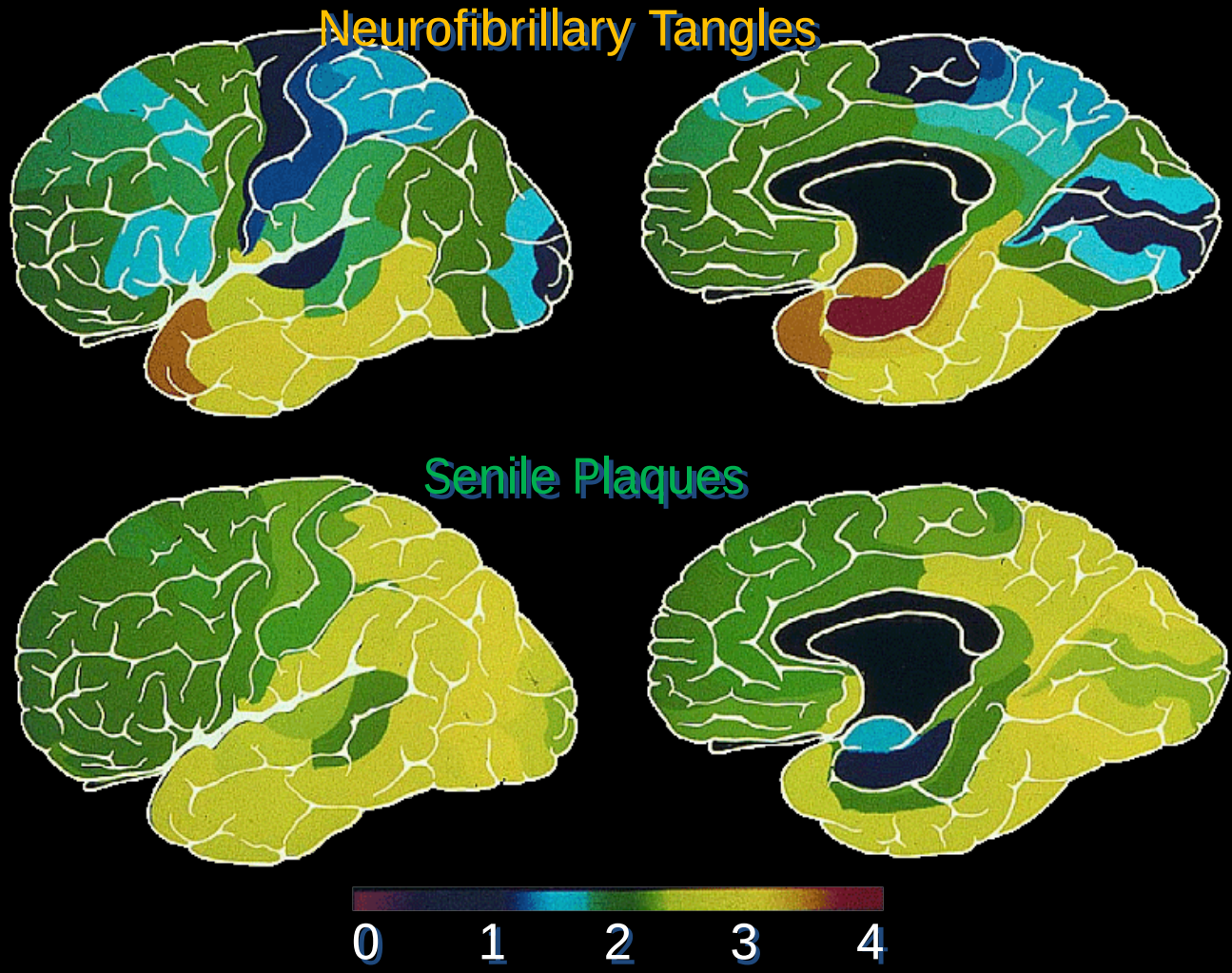
Salthouse, T.A. Psychon Bull Rev 2016: 23: 932-939.

Slowly progressive decline in cognitive ability: Normal aging, mild cognitive impairment – dementia



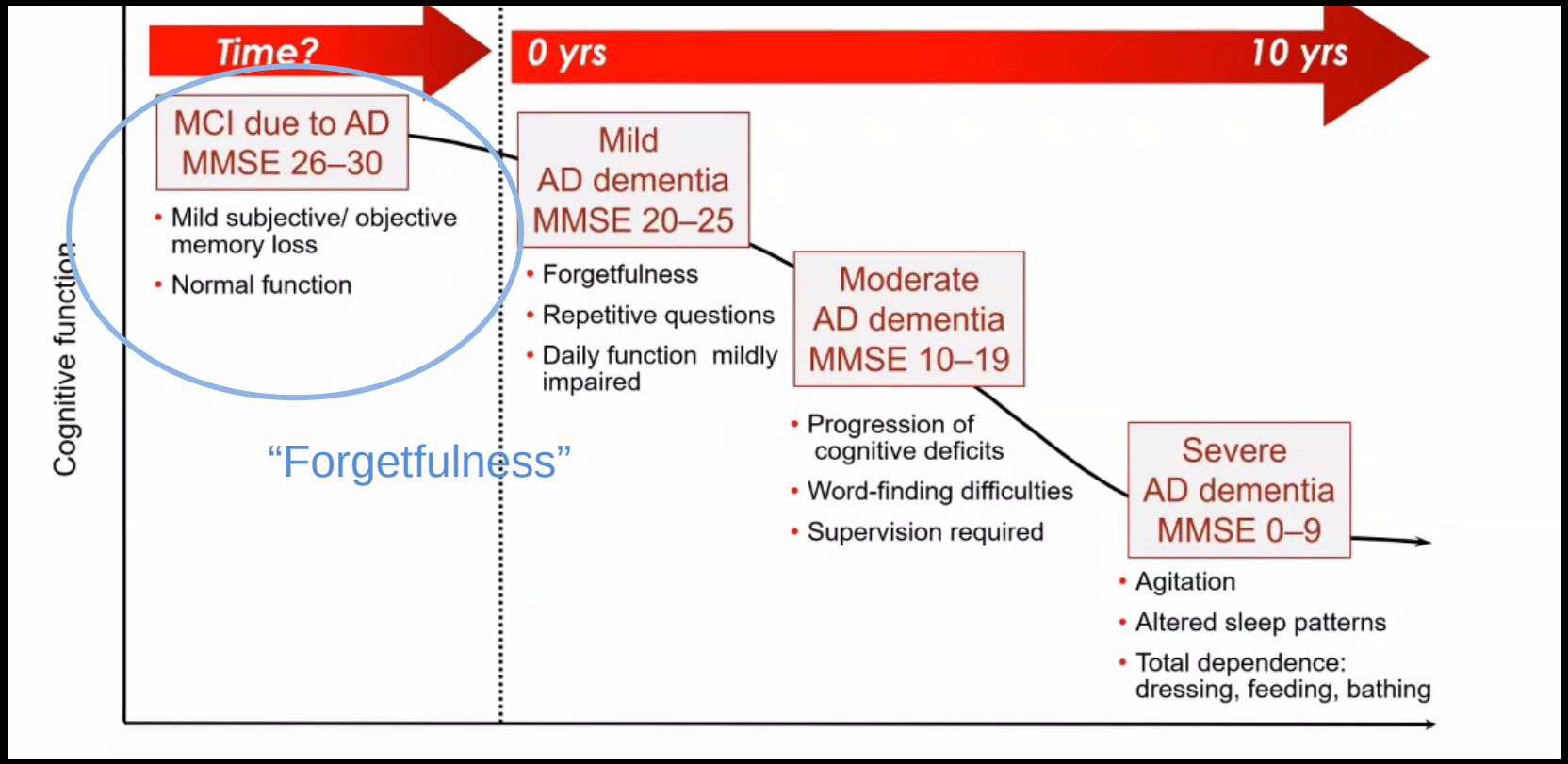
Topographical Distribution of AD Lesions





Arnold et al. *Cerebral Cortex*. 1991;1:103-116.

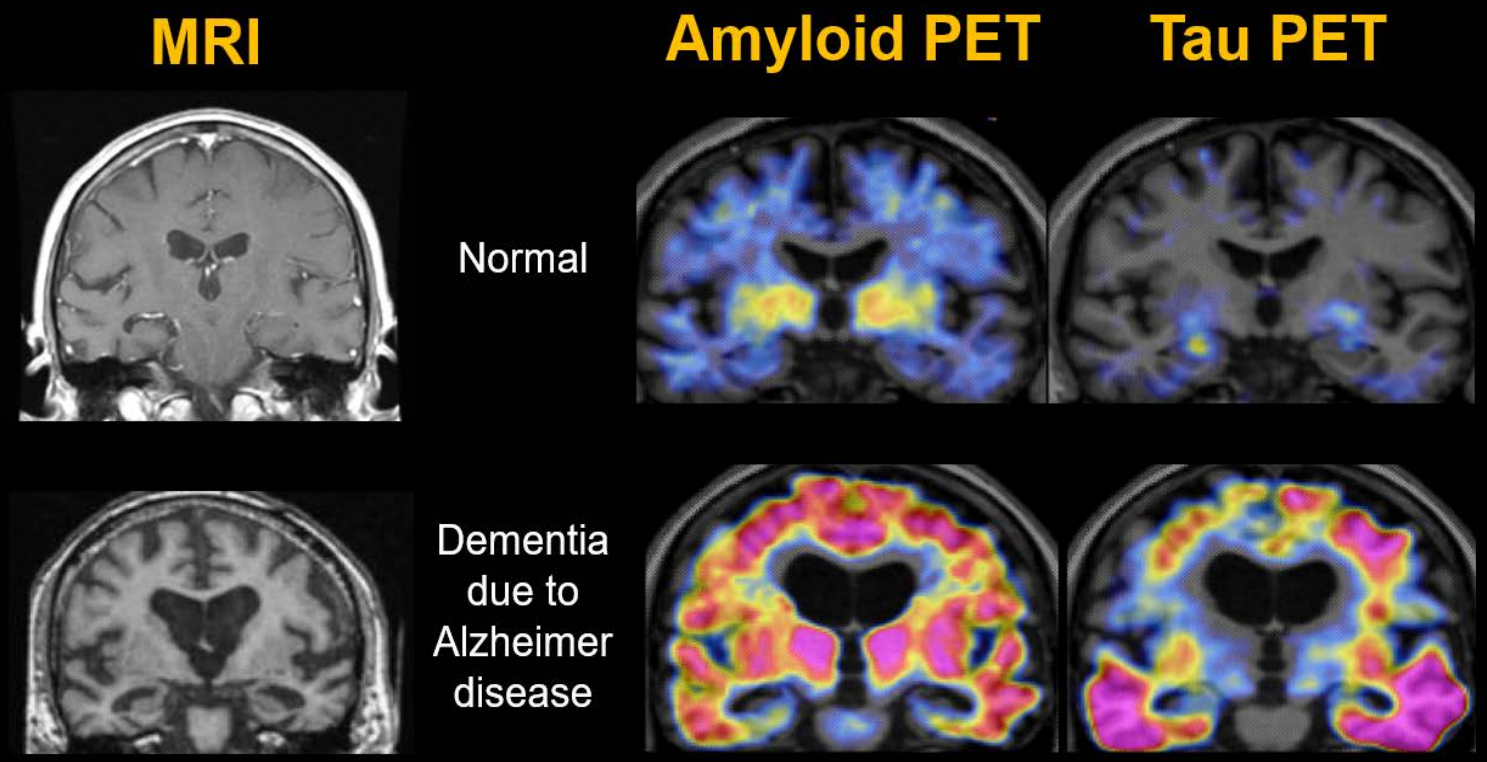
Symptomatic Progression of MCI and dementia due to Alzheimer Disease



Courtesy Paul Aisen MD

Brain Imaging in the Diagnosis of AD

Clinical Diagnosis — FDA-approved, but not paid by insurance



β-Amyloid and p-tau proteins can also be measured in spinal fluid and blood.

Johnson K. Ann Neurology 2016

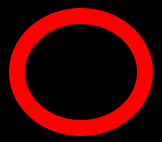
Varieties of Forgetfulness

- The Memory System
- The Spectrum of Forgetfulness
  - Severity and Causes
  - Prevention and Treatment

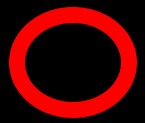
Prevention and Treatment

- Prevention and Risk Reduction
  - Genes matter
  - Reduce modifiable risk factors
  - Adopt Healthy Lifestyle
    - Aerobic Exercise
    - Mediterranean diet
- Treatment for MCI or dementia due to “AD”
  - Symptomatic treatment
  - Disease-modifying treatment?

Genetic Risk for AD depends on frequency and strength of the allele

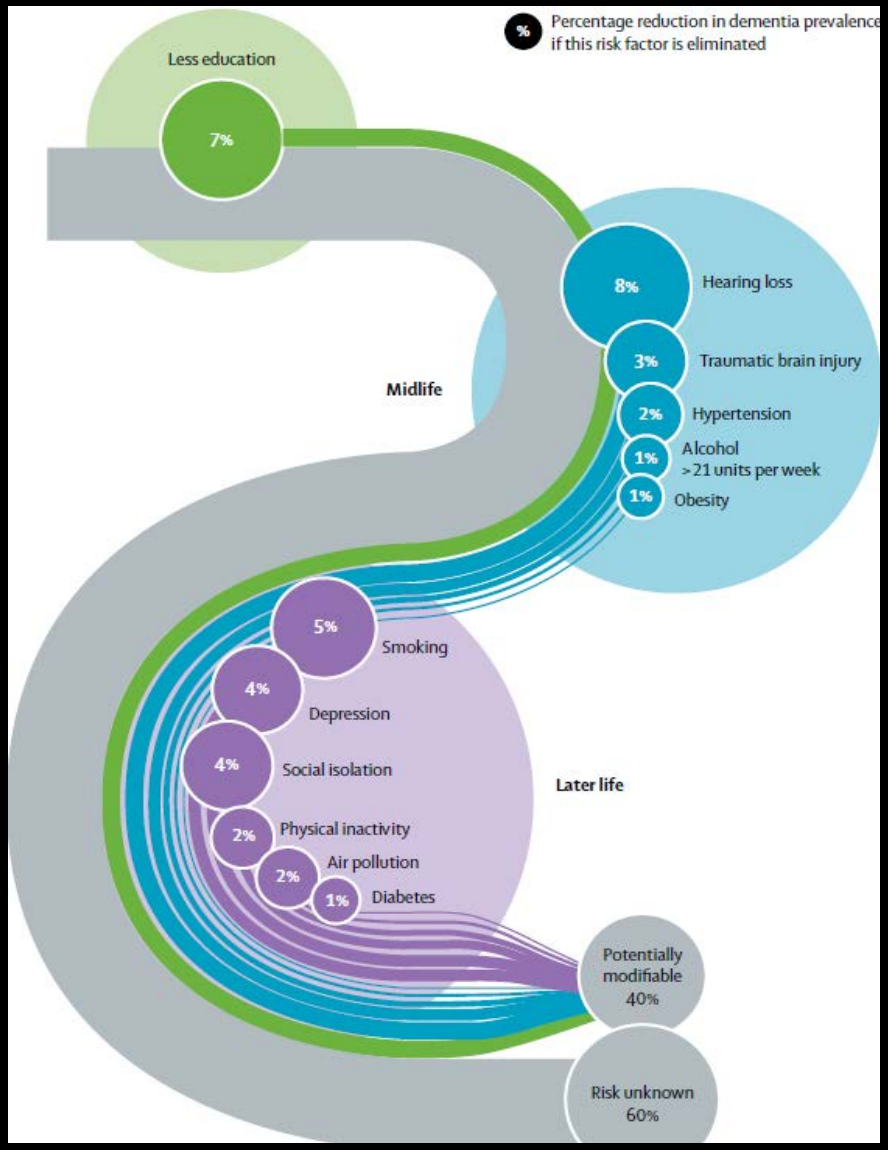


Apolipoprotein E4 accounts for the greatest genetic population attributable risk for AD



Karch CM & Goate AM. Biol Psych 2015; 77: 93.

12 Modifiable Risk factors for Dementia



- Modifying risk factors might prevent or delay up to 40% of dementias
  - Hearing loss = 8%
  - Smoking = 5%
  - Social isolation = 4%
  - Depression = 4%
  - Hypertension = 2%
  - Physical inactivity = 2%
  - Diabetes = 1%

Livingston G et al. Lancet 2020;396:413-446.

Commonly prescribed medications with cognitive side effects (Beers Criteria 2019)

Anti-cholinergics – urinary frequency

Benzodiazepines – insomnia, anxiety

"Z drugs" – insomnia

Anti-psychotics (1st generation) – hallucinations, confusion

Anti-histamines (1st generation) – allergies

Anti-depressants (1st generation) - depression, anxiety

J Am Geriatr Soc 2019; 67: 674-694

AHA/ASA life's simple 7

Lifestyle modifications:

1. Smoking status
2. Physical activity
3. Weight
4. Diet
5. Blood glucose
6. Cholesterol
7. Blood pressure

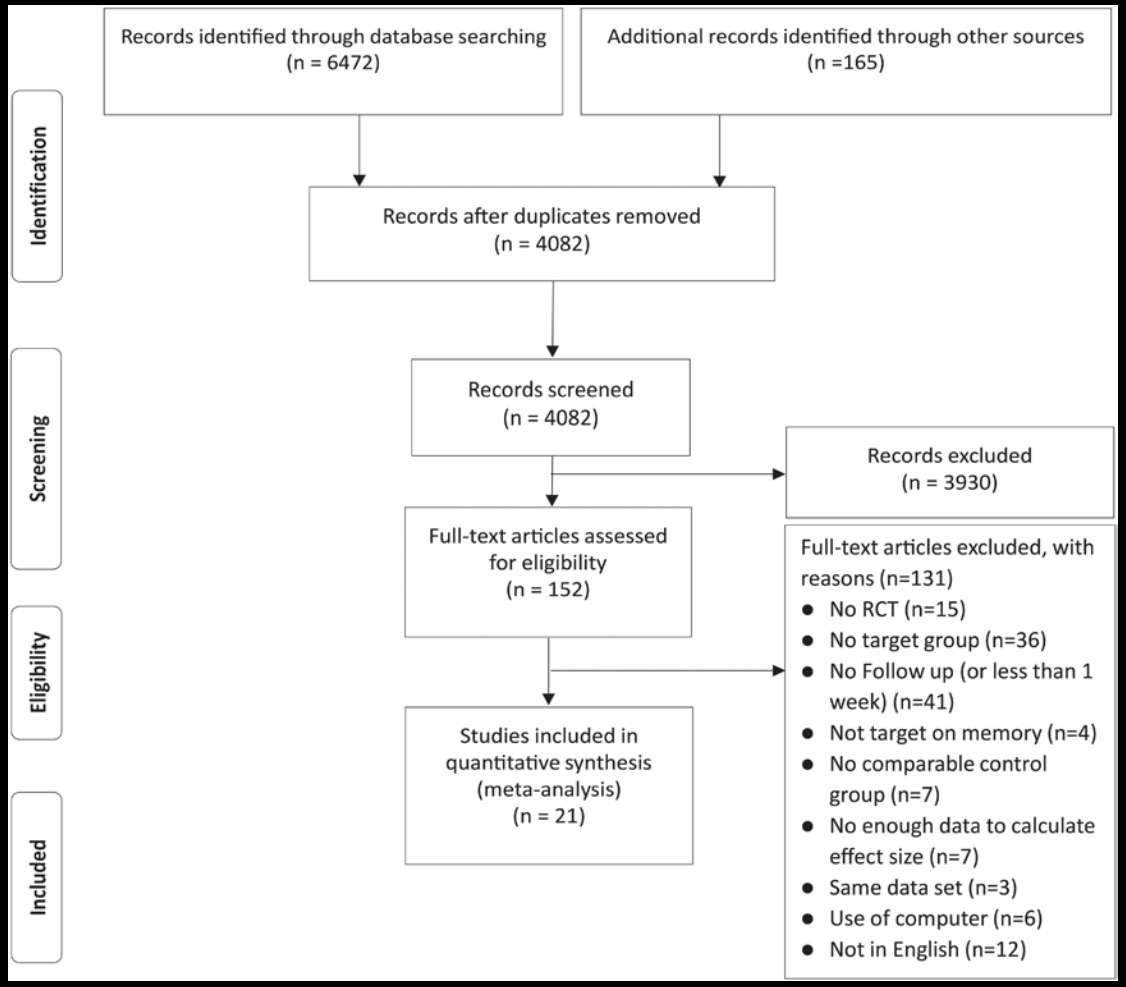
Vivrani SS, Circulation 2020;141:e139-e596.

Factor	Ideal Definition
Smoking status	Nonsmoker
Physical activity	Moderate-intensity activity >150min/week or vigorous intensity activity >75min/week or combination
Body mass index (BMI)	<25 kg/m2
Diet	1. Fruits and vegetables ≥ 4.5 cups/day 2. Fish ≥ two 3.5oz servings/week (preferably oily fish) 3. Fiber-rich whole grains (≥1.1g of fiber per 10g of carbohydrate) ≥ three 1oz equivalent servings/day 4. Sodium <1500mg/day 5. Sugar sweetened beverages ≤ 450kcal (36oz)/week
Fasting blood glucose	<100mg<dL (avoid hypoglycemia)
Total cholesterol	<200mg/dL
Hypertension	Untreated blood pressure <120/80 mmHg (avoid hypotension)

Mnemonic Training

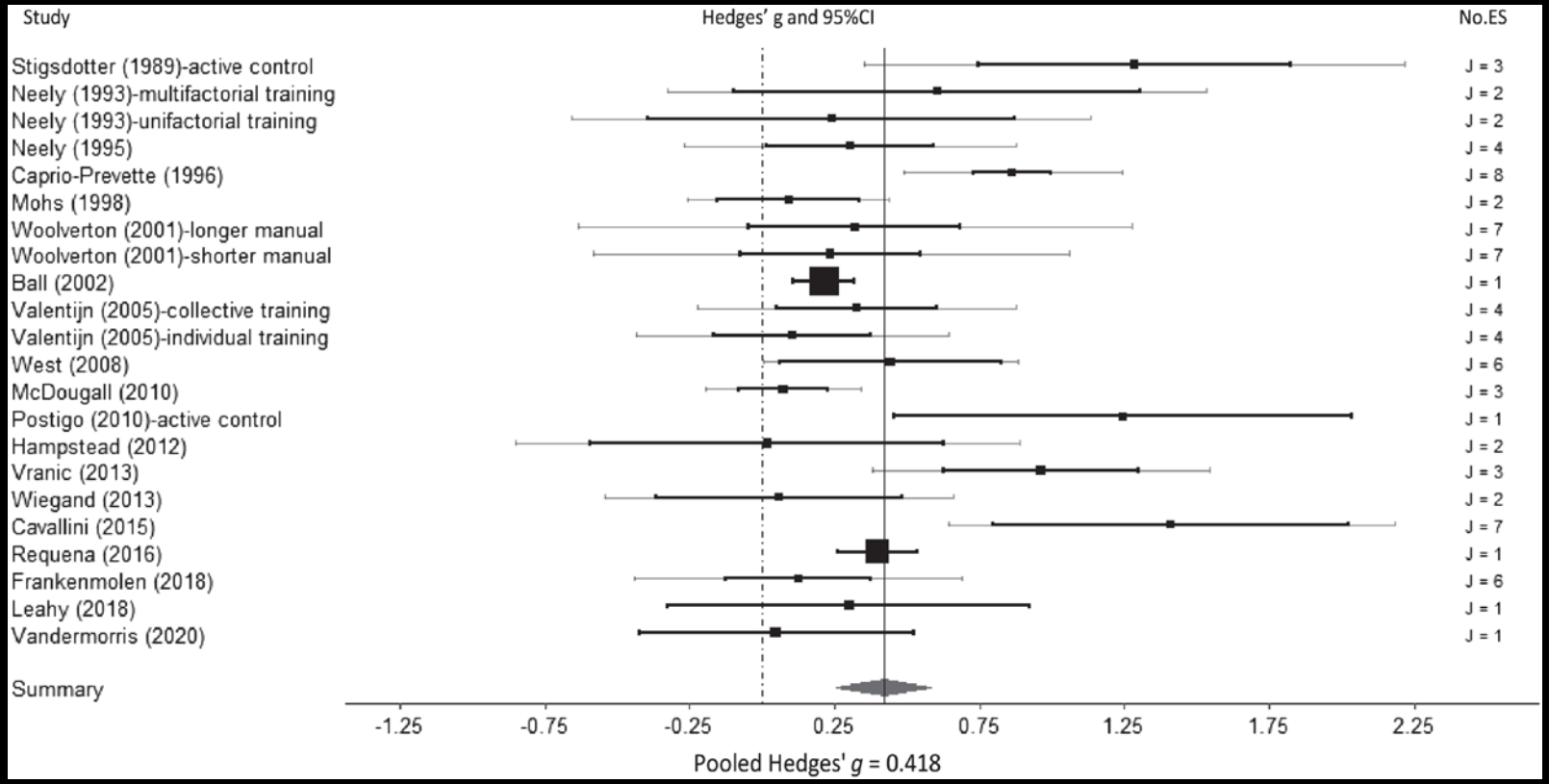
- Strategies
  - Chunking – semantic organization reduce memory load
  - Loci – associations based on well-established memory routes
    - learners to relate to-be-remembered information with such well-established routes during encoding so that they can mentally retrace their steps during retrieval (Yates, 2013).
  - External strategies - calendars and notes

Search for Studies that Qualify for Meta-Analysis



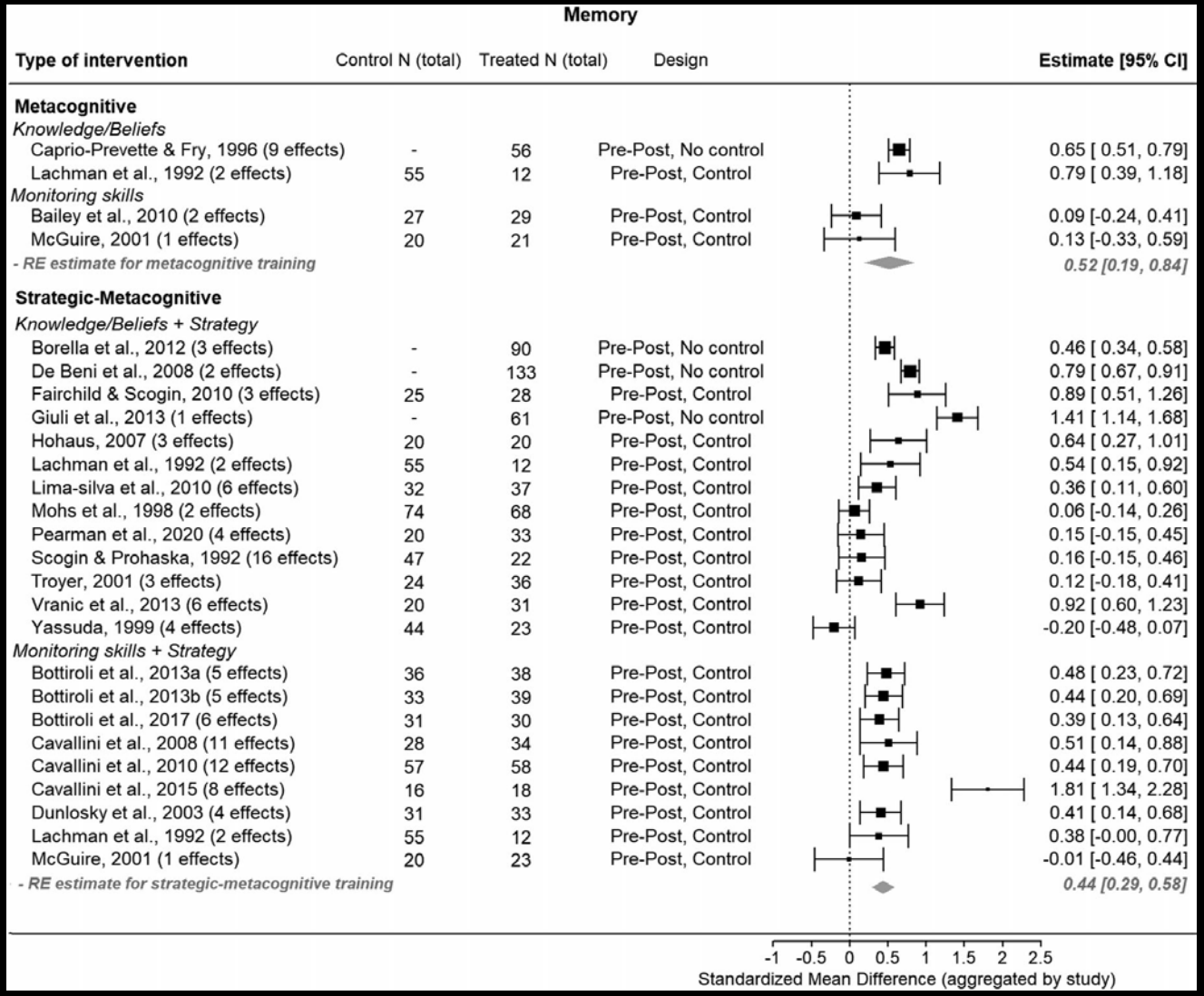
Chen, S. Psychology and Aging 2022.

Long Term Effects of Mnemonic Training in Normal Elderly Adults



Chen, S. Psychology and Aging 2022.

Effects of Cognitive Training in Normal Elderly Adults



Sella, E. Aging and Mental Health 2022; 10/12/1-12.

Effect of Physical Exercise on Global Cognition in Mild Cognitive Impairment

Biazus-Sehn. Arch Gero Geriatr 2020; 89: 104048

Medication that Increase Acetylcholine

12-month treatment effects

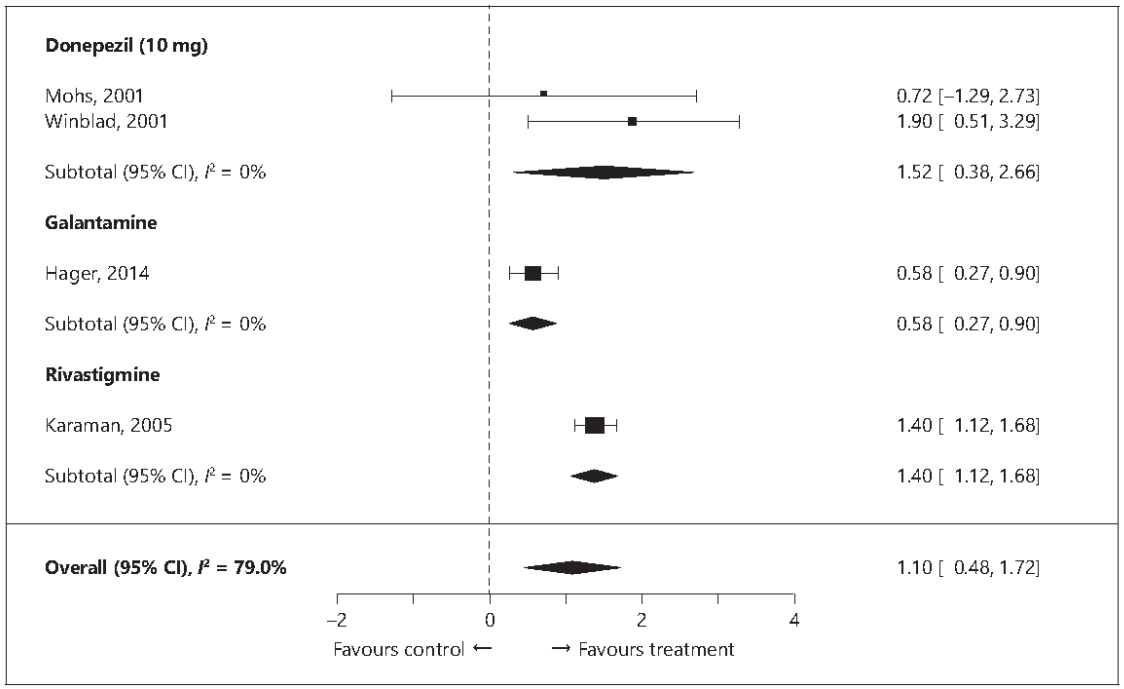


Fig. 5. Forest plot showing the treatment effects from the individual trials and meta-analysis results for acetylcholinesterase inhibitors at 12 months after treatment initiation. For the reference numbers of the studies, please refer to Table 1.

Knight R, Dementia Geriatric Cognititve Disorders 2018; 45: 131

The
University of Southern California
Memory and Aging Center
www.brainhealth.usc.edu

NIA Alzheimer Disease Research Center (ADRC)
California Alzheimer Disease Centers (CADC)

USC Health Care
Consultation Center
1520 San Pablo Street
Los Angeles, CA

Rancho Los Amigos
National Rehabilitation Center
7601 East Imperial Highway
Downey, CA